Infected arthritis due to *Blastocystis hominis*

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Abstract

A patient with rheumatoid arthritis taking prednisone developed *Blastocystis hominis* acute diarrhoea, which was associated with increased inflammation and effusion of the left knee. *B hominis* organisms were found in synovial fluid from the left knee. The patient responded dramatically to metronidazole treatment. *B hominis* may become disseminated in immuno-suppressed patients with diarrhoea and may cause infective arthritis.

*Blastocystis hominis*, originally thought to be a yeast, has been reclassified as a protozoan. It is initially accepted as a harmless commensal in the intestinal tract, it is now reported as a pathogen. It has been associated with recurrent diarrhoea and at least one death. Diarrhoea due to *B. hominis* is suspected when large numbers of organisms are seen in the absence of other known parasitic, bacterial, or viral causes. Clinical disease may not be limited to diarrhoea, however, as we report a case of infective arthritis caused by *B. hominis* in a patient with rheumatoid arthritis.

Case report

A 29 year old woman was admitted to the University Hospital, Kingston, Jamaica, with a six month history of morning stiffness, pain and swelling of the proximal interphalangeal joints, elbows, ankles, knees, and temporomandibular joints. Before this she had had intermittent arthralgia of the proximal interphalangeal joints, ankles, and knees for about one year. She was diagnosed as having seronegative rheumatoid arthritis, and treatment was started with indomethacin. Because of poor response, prednisone 15 mg daily was added. Three weeks before admission she began to experience diarrhoea, with three to four soft to watery stools daily with occasional blood and mucus. This was associated with intermittent lower abdominal pain and vomiting. The joint pains and swelling had increased, especially in the knees.

Physical examination showed an ill looking, thin woman with mild anaemia and dehydration. Her temperature was 38.1°C. There were small lymph nodes in the left upper cervical region, axillae, and epitrochlear area. There was mild swelling and tenderness of the proximal interphalangeal joints, wrists, elbows, and ankles. Marked synovial effusions were detected in both knees but were most pronounced in the left.

Abdominal examination disclosed tenderness in the lower abdomen. Rectal examination was normal. Sigmoidoscopy showed mild to moderate erythema and oedema of the rectal mucosa. Histology of the rectal mucosa was non-diagnostic, however.

The haemoglobin concentration was 64 g/l with a hypochromic, microcytic blood film. The total leucocyte count was 8.1×10⁹ cells/l with 62% neutrophils, 36% lymphocytes, and 2% eosinophils. The erythrocyte sedimentation rate (ESR) was 150 mm in the first hour. Radiology disclosed unequivocal periarthritis osteoporosis in the hands, and mild joint space narrowing of the metacarpophalangeal joints and hips bilaterally. There were marginal erosions of the proximal interphalangeal and right metacarpophalangeal joints. The rheumatoid factor, anti-nuclear factor, and antibodies to double stranded DNA were negative. The total serum complement level was 1.95 g/l (normal 1.22–1.66 g/l). The HIV test was negative. Joint fluid aspirated from the left knee was turbid and the leucocyte count was 38×10⁹/l with 100% neutrophils.

Treatment was started with cefotaxime intravenously for presumed infective arthritis of the knee pending results of joint fluid, blood, and stool cultures. There was no improvement after five days. Routine aerobic and anaerobic cultures of blood, synovial fluid, urine, and endocervical swab were all negative. Examination of synovial fluid (light microscopy, trichrome stain) from the left knee showed *B hominis* organisms. Stool specimens also disclosed large numbers of *B hominis* organisms (>5 per high power field). Culture for salmonella, shigella, campylobacter, and other parasites was negative.

Drug treatment was switched to metronidazole 400 mg eight hourly for two weeks. The abdominal pain, diarrhoea, and left knee inflammation subsided over the next five to seven days. Repeat knee aspirate and stools were negative for *B. hominis*. There was no recurrence of the knee inflammation at follow up four months after discharge from hospital.

Discussion

Many parasitologists now recognise *B. hominis* as an enteric protozoan pathogen and several laboratories have reported the presence of the organism in stools. It is a cause of diarrhoea when large number of organisms are found in stools (five or more organisms per high power field). Trichrome stained preparations of fixed material are recommended for confirmation. *B. hominis* is spherical, 5 to 30 μm in diameter, with a thick slime capsule but no cell wall. It
contains a membrane bound central body or vacuole and numerous peripheral granules and nuclei in the surrounding cytoplasm.\textsuperscript{1, 2, 6} It is strictly anaerobic, grows optimally at 37°C, and is resistant to high concentrations of amphotericin B. The microscopical appearance of \textit{B. hominis} is sufficiently distinctive when large numbers are present.

Mild to moderate diarrhoea, colicky abdominal pain, nausea, vomiting, and fever have been described in affected patients.\textsuperscript{5-7} There are no accurate estimates of the prevalence of \textit{B. hominis}. In one centre the organism was reported in 11-6% of stool specimens.\textsuperscript{8} In another study \textit{B. hominis} was found in 12-3% of patients.\textsuperscript{8}

The patient described here had acute diarrhoea associated with abdominal pain and vomiting. \textit{B. hominis} in large numbers was the only pathogen found in stool. Although we did not examine for viral pathogens, it is most unlikely that her diarrhoea was virally induced. The good response to metronidazole also confirms \textit{B. hominis} as the infective agent and mitigates against a viral cause.

\textit{B. hominis} infective arthritis has not been described before. The patient had seronegative rheumatoid arthritis, fulfilling five of the seven revised American Rheumatism Association criteria.\textsuperscript{9} Radiological examination showed periarticular osteopenia and also mild joint space narrowing and early erosions. When these features occur in the early stages of rheumatoid arthritis they usually reflect a more aggressive type of disease. There was also involvement of the knees, and at presentation the inflammation of the left knee was out of proportion to the general activity of the rheumatoid process. \textit{B. hominis} was seen in moderate numbers in the synovial fluid, without any other identifiable organism. Immunosuppression with prednisone given for her rheumatoid disease might have contributed to the systemic dissemination of the organism from the gastrointestinal tract with resultant infective arthritis. The likelihood of infectious arthritis is greater if host resistance is impaired by prior disease or by treatment with drugs that interfere with defence mechanism. In addition, previous damage by an arthritic disease predisposes a joint to infection.\textsuperscript{10}

The severe anaemia was probably due in part to iron deficiency anaemia as indicated by the hypochromic, microcytic blood film. Blood loss from the upper gastrointestinal tract might have resulted from chronic anti-inflammatory analgesic and steroid intake.

The patient responded to metronidazole given for two weeks, without recurrence at follow up. A more prolonged course of treatment is usually recommended for infectious arthritis. The knee inflammation responded dramatically, however, and treatment was shortened without any adverse effects. A longer course is recommended for patients who respond slowly.

In many of the reported cases \textit{B. hominis} caused symptoms in patients with an underlying immunosuppressive disease.\textsuperscript{11, 12} In one series 56% of patients with blastocystis in stools, without other parasites or bacterial pathogens, had some underlying disease, representing a debilitated state with some degree of immunosuppression or deficiency.\textsuperscript{5}

In \textit{B. hominis} diarrhoea the organism may become disseminated in immunosuppressed patients and cause infectious arthritis. Careful analysis of synovial fluid is necessary when synovitis occurs. Treatment with metronidazole is effective.